REMARKS

Claims 15-46 are pending and rejected. Claim 29 was previously withdrawn. Claims 15 and 37 are amended.

CLAIM REJECTIONS UNDER 35 U.S.C. §112

Claims 15-46 are rejected under 35 U.S.C. §112 ¶1 as containing subject matter not described in the specification so as to enable one skilled in the art to make and/or use the invention. Specifically the Examiner states that the "target tissue is exposed to light such that the tissue itself is photosensitized."

Applicants have amended claims 15 and 37 to clarify that exposing the target tissue is to light to "activate the photosensitizer to injure" the target tissue. The tissue is not photosensitized but the photosensitizer is excited to produce radicals that cause cellular injury. This is supported at least on page 14, lines 17 to 20:

> In the process outlined in Fig. 1, the photoexcitation of the aromatic chromophore effects rapid intramolecular energy transfer to the sulfenate group, resulting in bond rupture and production of two reactive free radicals which cause cellular injury.

It is also supported at least on page 3, line 10, to page 14, line 3, For these reasons applicants request that the rejection be withdrawn.

Claims 15-46 are rejected under 35 U.S.C. §112 ¶1 as containing subject matter not described in the specification so as to enable one skilled in the art to make and/or use the invention, the claims are drawn to a method of performing a "photosensitizing procedure." The Examiner relies upon three issues.

The Examiner's first issue is whether one could expect similar results of decreased cell viability in Lewis carcinoma cells as demonstrated in a Declaration filed February 25, 2005, with an "E" conjugated sulfenate compound. Applicants respectfully assert that coupling of photoactive molecules to various biomolecules is well know to one skilled in the art as referenced at least on page 13, line 21, to page 14, line 16. Fluorescent dyes that are bound to antibodies and peptides have been successfully used to image tumors. The dyes attached to the biomolecules have retained their ability to be photoexcited and transfer energy that results in fluorescence. The activity of photoactivated compounds can be maintained after conjugated with a targeting biomolecule as described at least in Achilefu et al. (*Novel receptor-targeted fluorescent contrast agents for in vivo tumor imaging,* InvestigativeRadiology, 2000, 35(8), 479-485)(IDS Ref. AR) and Licha et al. (*New contrast agent for optical imaging: acid –cleavable conjugates of cyanine dyes with biomolecules,* Proceedings of SPIE, 1999, 3600, 29-35)(IDS Ref. FR). Thus applicants respectively assert that their inventive sulfenate derivatives also involve an energy transfer mechanisms to form radicals and it is reasonable to expect they will maintain these mechanism after being conjugated to an "E" substituent. Although Examiner cites the Bonnett reference where six of the compounds were not very effective in a photonecrosis assay, a seventh compound, however, did exhibit considerable activity in the assay. Furthermore, Bonnett did not disclose the details of how the compounds were prepared and if they had photoactivity after their preparation and before testing in the photonecrosis assay. The compounds may not have been active as a result of the preparation method. For these reasons applicants respectfully assert that it is reasonable to extrapolate from applicants'

para-nitrophenyl-*tert*-butyl sulfenate in the Declaration filed February 25, 2005, that a photosensitizer will maintain its properties.

The Examiner's second issue is whether "a quantity of 500 micrograms sulfenate compound per gram pancreas actually reaches the pancreas as suggested by claim 30." Applicants respectfully disagree with Examiner's interpretation of what claim 30 suggests.

Claim 30 recites the "effective amount of the sulfenate photosensitizer administered to the target tissue is in a range of 0.1 mg/kg body weight to 500 mg/kg body weight." Applicants respectfully assert that in the Examiner's example the term "per gram of pancreas" refers to an amount reaching a specific organ within a body. Applicants' term "mg/kg body weight" is the amount, or dose, administered to the entire body as known to one skilled in the art. This is supported at least on page 18, line 22, to page 19, line 8.

The Examiner's third issue is that applicants "have not demonstrated that photosensitization occurs when the sulfenate compound is combined with the Lewis carcinoma cells" and could be explained by Pasto's bond scission followed by hydrogen abstraction atoms from lipid molecules or membrane bound proteins on the cell. Pasto, however, does not describe any interactions with lipids or proteins and the photo-induced reaction described does generate, at least, alkoxy radicals. Furthermore, applicants have shown that activation of a photosensitizer decreases the viability of cells as shown in the Declaration filed on February 5, 2005.

In a fourth issue the Examiner questions "how to administer the conjugate to the target tissue", for example, which "E" does one use, and "undue experimentation" would be required to practice the invention. Applicants respectfully

disagree. Applicants have provided specific examples of the type of biomolecules to use to target a tissue. For example, steroid hormones for prostate and breast treatment and diagnosis of tumors such as that in the prostate and breast, and integrin receptor and plaque binding molecules for vascular disease treatment (supported at least on page 13, lines 8 to 18; and page 13, line 21, to page 14, line 16). Thus, applicants respectively assert that there is reasonable predictability that the compounds will accumulate in the target tissue especially because they have a targeting moiety.

Thus for at least these reasons applicants respectfully request that the rejection be withdrawn.

Claims 15-46 are rejected under 35 U.S.C. §112 ¶2 as being indefinite. Applicants respectfully disagree.

In regards to Claim 15 the Examiner asks what are the manifestations of a tissue that has been photosensitized. Applicants have amended claim 15 to recite exposing the tissue with light to "activate the photosensitizer to injure the tissue." As previously stated the tissue is not photosensitized, rather, the photosensitizer is excited to produce radicals that cause cellular injury. This is supported at least on page 3, line 10, to page 14, line 3, and page 14, lines 17 to 20.

In regards to claim 15 the Examiner requests the applicants to provide examples of a carbohydrate receptor binding molecule and a carbohydrate receptor. Applicants have attached three abstracts describing carbohydrate binding molecules and carbohydrate receptors. (Vera et al. Nucl. Med. Biol. 2001, 28(5), pp. 493-8, [(99m)Tc]MAG(3)-mannosyl-dextran: a receptor-binding radiopharmaceutical for sentinel detection; Baveye et al. Infect. Immun. 2000, 68(12), pp. 6519-25, Human

lactoferrin interacts with soluble CD14 and inhibits expression of endothelial adhesion molecules, E-selectin and ICAM-1, induced by the CD14-lipopolysaccharide complex; Zimmermann-Belsing et al., Mol. Cell Endocrinol. 2002, 188(1-2), pp. 241-51, The influence of alpha1-acid glycoprotein (orosomucoid) and its glycoforms on the function of human thyrocytes and CHO cells transfected with the human TSH receptor)

In regards to claim 29 where "E" is associated with one of the biomolecules and a dendrimer, applicants withdrew claim 29 in the Supplemental Amendment filed June 21, 2005.

In regards to claim 30 the Examiner asks what is meant by the amount which is administered to the target tissue can be as high as 500 mg/kg body weight. As previously stated, applicants term "mg/kg body weight" is the amount, or dose, administered to the entire body as known to one skilled in the art. This is supported at least on page 18, line 22, to page 19, line 8.

In regards to claims 30-33 and 40-43 and the term "about", applicants deleted this term from the claims in an Amendment filed February 25, 2005.

In regards to claims 32-36 and 42-46 the Examiner's position is that they imply that the sulfenate is administered as a composition. Applicants have amended independent claims 15 and 37, from which claims 32-36 and 42-46 depend, respectively, to recite an effective amount of sulfenate photosensitizer "in a formulation." This is supported on page 18, line 14, to page 19, line 6, hence applicants assert that no new matter has been inserted.

For the above reasons applicants respectfully request that the rejection be withdrawn.

CONCLUSION

For the foregoing reasons, applicants believe that they have complied with the Examiner's request in his Communication, and submit that all the rejections have been overcome and that the application is in complete condition for allowance.

Applicants authorize the Commissioner to charge Deposit Account No. 23-3000 $1020, the fee for three months extension of time and do not believe any other fee is due with this submission. If any additional fees are necessary, the Commissioner may consider this to be a request for such and charge any necessary fees to Deposit Account No. 23-3000.

The Examiner is invited to contact applicants' undersigned representative with any questions.

Respectfully submitted,

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